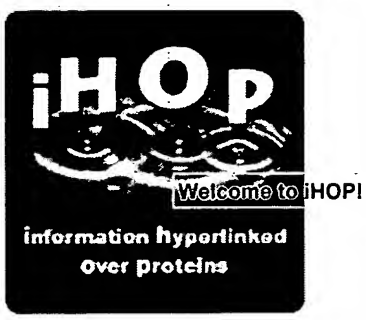

Symbol	Name	Synonyms	Organism
BIK	BCL2-interacting killer (apoptosis-inducing)	Apoptosis inducer NBK, BBC1, Bcl-2 interacting killer, BIP1, BP4, NBK	Homo sapiens

UniProt	Q13323, Q16582, Q6FH93
OMIM	603392
NCBI Gene	638
NCBI RefSeq	NP_001188
NCBI RefSeq	NM_001197
NCBI UniGene	638
NCBI Accession	CAA62013, CR541863

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METHODS: Human FcepsilonRI alpha chain, a human monoclonal allergen-specific **IgE** antibody (chimeric **Bip 1**), and the corresponding allergen, the major birch pollen allergen Bet v 1, were produced as recombinant proteins and analyzed by means of circular dichroism and native overlays, respectively.

Surprisingly, mutation of the **AP-1** site did not produce significant alteration in the activity of the **BP4** promoter.

Collectively, the results identify **BIK**✩ as an initiator of cytochrome c release from **mitochondria** operating from a location at the ER.

Deletion of a 25 bp sequence from -872 to -848, which contains the **AP-1** site, significantly reduced **BP4** promoter activity by approximately 50%.

We therefore examined the role of the single **AP-1** site (-869/-863) and other cis elements, in regulating the expression of **hBP4** gene, in the current studies.

This benzyloxycarbonyl-Val-Ala-Asp-fluoromethylketone-insensitive pathway for stimulating cytochrome c release from **mitochondria** by ER **BIK**✩ was successfully reconstituted in vitro and identified the requirement for components present in the light membrane (ER) and cytosol as necessary for this activity.

A significant fraction of **BIK**✩, which contains a predicted transmembrane segment at its COOH terminus, was found inserted in the **endoplasmic reticulum** (ER) membrane, with the bulk of the protein facing the cytosol.

We have previously reported the isolation and preliminary characterisation of a full-length **cDNA** sequence derived from the human **BBC1 [?]** gene, a gene which displays differential expression in tumours of the female breast [Adams et al., Hum. Mol. Genet. 1 (1992) 91-96].

The IGF **BP-4** **mRNA** levels in flight cultures were 75% lower than in

Concept & Implementation

by Robert Hoffmann

ground controls on the fifth day but were not different on the fourth day.

His-tagged recombinant (r) **Bip 1** Fabs were isolated by nickel **affinity chromatography** and rBip 1 Fabs without His-tag were purified via affinity to rBet v1. rBip 1 Fabs with and without His-tag bound specifically to rBet v1 and, like Bet v1 -specific human serum IgE and rabbit-anti rBet v1 antibodies, cross-reacted with Bet v1-related allergens in other plant-species (alder, oak, hazelnut).

Bip 1 Fabs displayed a cross-reactivity to homologous **allergens** comparable with that of IgE Abs from allergic patients.

Nonapeptides selected by phage display mimic the binding sites of **monoclonal antibodies** **BIP1** and BIP4 on Bet v 1, the major birch pollen allergen.

In **immunoblotting** experiments, antibody **BIP 1** reacted with a 17-kilodalton (kD) protein considered to represent the major birch pollen allergen Bet v I.

Like Bax and Bak, **Nbk** was cloned from a yeast two-hybrid screen for **proteins** that interact with E1B 19K.

Selections were performed with **BIP 1**, a murine monoclonal antibody known to enhance the **IgE** binding to Bet v 1, and with anti-Bet v 1 **IgE** purified from patients' sera.

Results: With the three-dimensional epitope search it became possible to localize a discontinuous **IgE** epitope on the surface of Bet v 1 in a substantial distance from the **IgG** epitope of the monoclonal antibody **BIP 1**.

BH-3-only **BIK** functions at the **endoplasmic reticulum** to stimulate cytochrome c release from **mitochondria**.

The modified **Bip1** heavy chain **cDNA** was co-expressed in E. coli XL-1 Blue with the Bip 1 light chain **cDNA** using the combinatorial plasmid pComb3H.

The mRNAs for both rIGFBP-3 and rIGFBP-4 were present in GH3 cells; T3 treatment increased steady state levels of rIGFBP-3 **mRNA**, but did not affect **BP-4** **mRNA** levels.

top

We report here that the pure antiestrogen ICI 182,780 and, to a lesser extent, the commonly used drug **tamoxifen** significantly increase levels of a M(r) 43,000-46,000 **IGFBP** (BP-3) and significantly reduce levels of a M(r) 24,000 **IGFBP** (**BP-4**) in the **conditioned medium** of MCF7 cells.

Immunization with **BIP 1** mimotopes induced **IgG** enhancing the **IgE** binding to Bet v 1, whereas immunization with **IgE** mimotopes resulted in **IgG** capable of blocking human **IgE** binding in vitro.

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☐	L13	(Apoptosis ADJ inducer ADJ NBK) OR BBC1 OR (Bcl-2 interacting ADJ killer) OR BIP1 OR BP4 OR NBK AND cancer	5266
☐	L12	BCl-2 AND bik and cancer and (therapy or administer or treat)	259
☐	L11	((BCL-2 or bik)) AND ((cancer or proliferative) AND serine)	2012
☐	L10	((BCL-2 AND bik))[AB]	2
☐	L9	((Bik OR nbk OR blk))[AB] AND (cancer AND serine and threonine)	21
☐	L8	L7 and serine and threonine	253
☐	L7	L6 AND administer	410
☐	L6	(Bik OR nbk OR blk) AND cancer	1188
☐	L5	(Bik ORnbk OR blk) AND cancer and administer	400
☐	L4	L1 and administer	58
☐	L3	L1 and Akt	48
☐	L2	L1 and therapy	161
☐	L1	Bik and cancer and threonine and serine	176

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